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Anti-TNF therapy (etanercept, infliximab and adalimumab) for rheumatoid arthritis

Anti-TNF is a name given to a new class of drugs available for the treatment of severe rheumatoid arthritis. Currently this group consists of three drugs, infliximab (trade name Remicade), etanercept (trade name Enbrel) and adalimumab (trade name Humira). These drugs work by blocking the action of TNF (tumour necrosis factor) a molecule responsible for increasing levels of inflammation in people with rheumatoid arthritis.

Etanercept is currently prescribable for both children and adults, whereas infliximab must be prescribed with methotrexate and is only licensed for the treatment of adults. Infliximab is now also licensed for ankylosing spondylitis. See **arc** informations sheets etanercept, infliximab and adalimumab for further information.

Adalimumab, which received its licence in September 2003 is also only licensed for adults and can be take with or without methotrexate, although to ensure maximum efficacy adalimumab should be taken in conjunction with methotrexate.

Anti-TNF therapy has recently been evaluated by the National Institute for Clinical Excellence (NICE), which has recommended that the therapy should be prescribed in line with the following guidance, provided by the British Society for Rheumatology.

Guidelines on the prescribing of anti-TNF therapy

- You must have been treated with at least two DMARDs (disease-modifying drugs – examples of these are; gold injections, sulphasalazine, hydroxychloroquine, leflunomide, cyclosporin, azathioprine and methotrexate). One of the two must be methotrexate. Your consultant must be of the opinion that your condition was not suitably controlled by these drugs, either because your symptoms were not reduced to the consultant's satisfaction, or because of adverse side-effects.
- You must have active rheumatoid arthritis, which can be measured on a score of 'disease activity' in your joints. To be considered for anti-TNF you must reach a certain score on this scale, which will be determined through two visits to the rheumatology department, usually one month apart. People whose disease does not reach a certain point on the DAS (disease activity score) may not be considered for anti-TNF.

It should be noted that both anti-TNF drugs are not suitable for everyone, and people with some pre-existing conditions may not be eligible for the treatment. As with all drugs, they also carry a risk of adverse effects.

Frequenty asked questions

Are these drugs available as tablets? How do I take them?

No, unfortunately, because of the method of action of anti-TNF, it is not possible at present to make these drugs available in tablet form. Etanercept and adalimumab are injected under the skin, at home. Etancercept is injected

twice a week and adalimumab once a fortnight, by either yourself or a helper. Infliximab is given via an infusion (drip) in hospital at regular intervals. Your rheumatology department can provide further information about the administration of these drugs.

I have had problems with side - effects following treatment with methotrexate. Do I have to take anti-TNF medication with methotrexate?

Yes, at present infliximab and adalimumab are usually prescribed with methotrexate. However, etanercept and adalimumab can be taken without other DMARDs. You should discuss both options with your rheumatologist who should be able to advise on suitability.

Can I get these drugs from my GP?

No. Anti-TNF drugs should only be prescribed and monitored by a rheumatologist.

I have osteoarthritis. Will these treatments work for me?

No. Osteoarthritis and rheumatoid arthritis are two completely different disease processes, and while anti-TNF may help to alleviate the inflammation of rheumatoid arthritis, it has no effect on degenerative conditions such as osteoarthritis and anti-TNF is not licensed for the treatment of osteoarthritis.

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Highlights from the 2002 American College of Rheumatology National Scientific Meetings

osteoarthritis – epidemiology

Allan Gelber, M.D., M.P.H and Shari Ling, M.D.

The following abstracts were written by Allan Gelber, M.D., M.P.H

Abstract 1227 **Serum Hyaluronic Acid Levels and Radiographic Knee Osteoarthritis in African-Americans and Caucasians.**
JM Jordan, G Luta, T Stabler, JB Renner, AD Dragomir, MC Hochberg, CG Helmick, VB Kraus.

In the field of osteoarthritis research, there has been much interest in defining a valid biomarker of disease. One potential biomarker is the serum level of hyaluronic acid – a compound found in cartilaginous tissues. Jordan et al investigate the relationship of serum hyaluronic acid to knee and hip osteoarthritis among 761 participants in the Johnston County Osteoarthritis Project.

Results: The investigators found that serum hyaluronic acid was in fact strongly associated with the presence of radiographically-evident osteoarthritis, at both the knee and hip joints. Moreover, higher levels of serum hyaluronic acid were observed in Johnston Country residents with more severe radiographic evidence of osteoarthritis. These associations persisted after taking age, race and gender into account in the analyses. These findings provide strong evidence that serum hyaluronic acid is a biomarker for prevalent osteoarthritis.

Editorial Comments: It remains of much interest to know if serum hyaluronic acid may also be predictive of the development and of the progression of osteoarthritis.

Abstract 962 **Inflammation markers (CRP, TNF-a, IL-6) are not associated with radiographic or MRI findings of knee OA in the elderly: The Health ABC Study**
M Nevitt, D Felson, C Peterfy, K Wildy, S Ling, N Lane, A Newman, L Carbone, T Harris.

A generation ago, osteoarthritis was considered to be an entirely degenerative disorder, the result of aging-related "wear and

tear" to the joints. Subsequently, increasing laboratory evidence supported a role for inflammation in the pathogenesis of osteoarthritis, with excess proliferation of inflammatory cytokines and of degenerative metalloprotease enzymes in osteoarthritic joints. In this light, investigations have sought to determine if serum markers of inflammation may be indicative of the presence of osteoarthritis or predictive of its future development.

Methods: To address this issue, Nevitt et al examined the relationship of serum levels of several inflammatory markers, including CRP, TNF-a and Il-6, to x-ray and MRI evidence of knee osteoarthritis. These features were studied in a large biracial community cohort of men and women, living in Memphis and Pittsburgh.

Results: Among 684 knees for which inflammatory markers, x-ray and MRI data were available, no overall differences were observed in levels of the markers of inflammation in those with compared to those without osteoarthritis. Therefore, this study failed to find a relationship between inflammation markers and radiographic evidence of osteoarthritis.

Editorial Comments: Of note, this study only examined the relationship of such markers to prevalent osteoarthritis and therefore do not address the relationship of these markers in young or mid-adult life to the risk of developing osteoarthritis later in life.

Abstract 965 **Squatting in daily living increases the prevalence of knee OA among Chinese elderly: The Beijing Osteoarthritis Study**
Y Zhang, L Xu, M Nevitt, J Niu, L Lui, W Yu, P Aliabadi, D Felson.

Prior work from this investigative team has demonstrated that the prevalence of knee osteoarthritis is similar in Chinese men, and even higher among Chinese women, compared to Caucasians in the United States. This earlier finding was surprising given the higher prevalence of overweight and obesity, a major risk factor for knee osteoarthritis, in the United States compared to China. The investigators speculated that more frequent daily squatting, by virtue of the deleterious biomechanical forces exerted upon the knee joint during squatting, might explain this higher than expected burden of knee osteoarthritis in the Chinese population.

Results: The frequency of squatting in relation to the prevalence of osteoarthritis was examined among 1843 Chinese elderly aged 60-89 years was examined by Zhang and colleagues. In the Beijing participants, 41% of men and 69% of women reported that at age 25 they had squatted an hour or more per day. A clear relationship between squatting to radiographic evidence of knee osteoarthritis was in fact demonstrated. Knee osteoarthritis was most prevalent among men who squatted 2 or more hours per day, and was similarly most prevalent among

Chinese women who squatted 3 or more hours per day. Moreover, squatting was more strongly associated with bilateral than with unilateral knee osteoarthritis. The investigators also concluded that squatting accounts for a relatively large proportion of the difference in prevalence of knee osteoarthritis between Chinese elderly in Beijing and Caucasian Americans.

Editorial Comments: One limitation of this study is the accuracy of squatting recall in an elderly population. There exists the potential for those elderly suffering from knee osteoarthritis to be more apt to recall greater squatting activity when they were young. It remains of interest to know the predictive relationship of squatting to future development of knee osteoarthritis in the Chinese population has not been examined.

Abstract 1232 **Are Mexican Americans at High Risk for Hip and Knee Osteoarthritis**
A Escalante, MJ Lichtenstein, HP Hazuda

Uncertainty remains as to whether racial disparities in osteoarthritis prevalence exist. Previous studies have predominantly focused on African Americans and Caucasian populations. Relatively few data are available regarding the prevalence of knee and hip osteoarthritis in Hispanic and Mexican Americans.

Methods: Escalante et al examined the prevalence of osteoarthritis risk factors in the San Antonio Longitudinal Study of Aging. For example, obesity was more prevalent (mean BMI of 29.3 k/gm2) among the Mexican Americans than in the non-Hispanic white participants (mean BMI of 27.6 kg/m2). On the basis of such figures which were next applied to the 1st National Health and Nutrition Examination Survey dataset, the investigators estimated, using statistical modeling, what the prevalence of knee and hip osteoarthritis would be in the Mexican American and non-Hispanic white populations living in San Antonio.

Results: Based upon this modeling, the prevalence of radiographic hip osteoarthritis would be 4.8% among Mexican Americans and 3.7% among non-Hispanic whites. Similarly, the prevalence of knee osteoarthritis would be 17.8% among Mexican Americans and 12.6% among non-Hispanic whites.

Editorial Comments: While these findings provide support for concluding that knee and hip osteoarthritis is in fact more prevalent in Mexican Americans, actual data as opposed to computer modeling-derived evidence remain unavailable to fully confirm this conclusion.

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The following abstracts were written by Shari Ling, M.D.

Abstract 298 **Relationships between spinal OA, vertebral fracture and bone mass. The Rancho Bernardo Study.**
Grigorian M, Schneider DL, Fem Bo et al. (see osteoporosis highlights)

Abstract 1233 **Age and gender alter the relationship between radiographic osteoarthritis of the knee and bone mineral density: Data from the Baltimore Longitudinal Study on Aging**
SM Ling, EM Simonsick, M Lethbridge-Cjeku, MC Hochberg, EJ Metter.

This study examined the association between bone density and radiographically defined OA of the knee (KOA) using data from the Baltimore Longitudinal Study on Aging (BLSA). 230 BLSA participants with KOA (189 with OA at baseline and 41 who developed OA over a 10 year period) were compared to the 211 who remained free of KOA over a 10-year follow-up interval.

Results: Femoral neck or trochanter BMD was not associated with KOA in women. In men, higher KL grade was associated with higher femoral neck BMD (KL 2 B= 0.07, p< 0.01; KL 3 - 4 b= 0.23, p < 0.001). Interaction terms for age*severity were inversely related to femoral neck BMD (KL 2*Age B= -0.004, KL 3-4*Age (B= -0.012; p < 0.01)-that is, BMD was higher with higher KL grades in younger subjects and lower in older subjects with higher KL grades. Similar trends were observed for greater trochanter BMD. These data suggest that the relationship between OA and BMD is complex, in that it differs in men and women, and varies with age.

Editorial Comment: The interaction between age and KL grade implies that the relationship between OA and BMD is altered by age. That is, younger men with OA have higher BMD while older men with OA have lower BMD.

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